REMARKS

Entry of this paper and consideration of the subject application in view thereof are respectfully requested.

Claims 1-12 were pending in this application. Claims 1-6 are under examination and claims 7-12 have been withdrawn from further consideration as being directed to non-elected invention. Claims 1-6 stand rejected. Claims 1 and 5 have been amended to clarify the invention. No new matter is added by these amendments.

Response to Rejection Under 35 U.S.C. §101

Claims 1-6 stand rejected under 35 U.S.C. § 101 as allegedly lacking a well-established utility.

At the outset, Applicant respectfully points out that the Examiner's rejection under 35 U.S.C. § 101 runs afoul of the established patent examining procedure. Specifically, the rejection of claims for the first time in the Office Action is improper given that the claimed subject matter has been entered into the record of the above application and the Office has already issued an office action on the merits (see paper number Paper No. 20050112 issued prior to the present Office Action) since the entry of the claimed subject matter. Such a practice constitutes piecemeal examination forbidden by MPEP §707.07(g). The piecemeal examination deprived Applicant's opportunity to have its application efficiently examined in a timely manner.

As to the merits of the rejection, Applicant respectfully traverses the rejection and submits that the claimed methods and cells have "real world" utility as well as specific and substantial and credible utility. The present invention is directed to, among other things, foreign protein-expressing cells comprising a GPCR and a chimeric Gq α subunit consisting of, from N-terminus to C-terminus, amino acid sequence of Gq α or $G_{11}\alpha$ subunit N-terminal region encompassing $\beta\gamma$ subunit activation site and amino acid sequence of $G_{14}\alpha$, $G_{15}\alpha$, or $G_{16}\alpha$ subunit C-terminal region encompassing receptor binding site. The Examiner takes the position that the claimed cells and methods of making the cells comprise orphan GPCRs with unknown functions. Notwithstanding, the claimed cells are useful for identifying a ligand for the GPCR with unknown functions. Finding ligands for potential new therapeutics is perhaps one of the most important facets of drug discovery. According to the present invention, whether a test substance is a ligand for the GPCR or not can be determined by a single assay

technique, including an assay based on changes in Ca-dependent Cl current as indicators of intracellular Ca concentration, regardless of the type of GPCR to which the ligand binds (see page 5 lines 2 to 5). Thus, the present invention enables simplification and acceleration of the assay method for identifying a ligand for a GPCR with unknown functions (see page 6 lines 17 to 19). See also the working examples, for example, at page 8 lines 17 to 22). Reconsideration and withdrawal of the rejection are respectfully requested.

Response to Rejections Under 35 USC § 112

Claims 1-6 stand rejected under 35 U.S.C. 112, first paragraph based on the assertion that a person of ordinary skill in the art would not know how to use the claimed invention. Applicant respectfully traverses the rejection. As discussed above, the claimed methods and cells have "real world" utility as well as specific and substantial and credible utility. There was also a high level of skill in the art at the time the instant application was filed. Given the enabling disclosure in the specification, a person skilled in this art would know how to use the claimed methods and cells for expressing a given GPCR. The expressed receptor is then screened in a variety of functional assays to look for an activating ligand as part of drug discovery. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-6 further stand rejected under 35 U.S.C. 112, first paragraph based on the assertion that these claims fail to comply with the written description requirement.

Specifically, the Examiner contends that there is no support for the recitation "that couple with G-proteins other than Gq subtype G-proteins." Without conceding the validity of this rejection and solely to expedite the prosecution of this application, Applicant has elected to strike the corresponding language from claims 1 and 5. Accordingly, reconsideration and withdrawal of the written description rejection are respectfully requested.

Response to Rejection Under 35 USC § 102

Claims 1-2 and 5-6 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Nakamura et al., 1996, J. Biochem., 120:996-1001. Applicant respectfully traverses this rejection for at least the following reasons.

The independent claims 1 and 5 require, among other things, co-expression of G-protein coupled receptors (GPCRs) and a chimeric Gqα subunit consisting of, from N-terminus to C-terminus, amino acid sequence of Gqα or $G_{11}\alpha$ subunit N-terminal region

encompassing βγ subunit activation site and amino acid sequence of $G_{14}\alpha$, $G_{15}\alpha$, or $G_{16}\alpha$ subunit C-terminal region encompassing receptor binding site.

The method claimed in, for example, claim 1 may be characterized in that genes encoding GPCRs and genes encoding a chimeric Gq α subunit consisting of, from N-terminus to C-terminus, amino acid sequence of Gq α or $G_{11}\alpha$ subunit N-terminal region encompassing βγ subunit activation site and amino acid sequence of $G_{14}\alpha$, $G_{15}\alpha$, or $G_{16}\alpha$ subunit C-terminal region encompassing receptor binding site are transfected into animal cells and expressed therein. Conventionally, when a ligand for a GPCR is determined, assay methods had to be altered in accordance with the G-protein subtype with which the GPCR couples; and, therefore, when the G-protein subtype with which the GPCR couples was unknown, it was necessary to try several assay methods (see, for example page 2 lines 4-22 of the specification). According to the present invention, however, regardless of what subtype of G-protein with which a GPCR couples, it is possible to elucidate a function of the GPCR by using a single assay technique, including an assay based on changes in Ca-dependent Cl current (see, for example, figure 4 and at page 8 lines 17-22). Figure 4 clearly shows that even GPCRs which couple with G-proteins other than Gq subtype G-protein can induce Ca-dependent Cl responses when the chimeric Gqα subunit is coexpressed. Figure 4 additionally shows that the responses are not induced when the chimeric Gqα subunit is not coexpressed.

Nakamura et al., studies that what type of chimera among several chimeras between $G_{L1}\alpha$ and $G_{L2}\alpha$ coexpressed with mGluR1 could effectively activate PLC (see, for example, Abstract and Figure 1 of Nakamura). Nakamura studies the combination of mGluR1, which is known to couple with Gq subtype G-protein, and chimeras shown in Figure 1. Nakamura, however, does not teach or disclose coexpression of GPCRs with unknown functions and chimeric G-proteins.

As to Hermans, this reference describes that mGluR1 is able to activate Gi and Gs subtypes of G-proteins aw well as Gq subtype G-protein (see Figure 3). Such multiple signaling pathways activation by one GPCR is commonly known. For example, some GPCRs which preferentially activate Gi subtype G-protein may activate Gq and/or Gs subtype G-protein. GPCRs have different affinities for different subtypes of G-proteins. In other words, some GPCRs preferentially activate one or several of G-proteins and do not preferentially activate others. For example, mGluR1 preferentially activates Gq subtype G-protein and does not preferentially actibate Gi and Gs subtypes of G-proteins by mGluR1,

since the activations are relatively weaker than that of Gq subtype G-protein, and an observer can substantially only detect activation of Gq subtype of G-proteins by mGluR1 by inactivating the activations of Gi and Gs subtypes of G-proteins by mGluR1 by inactivating the activation of Gq subtype (see page 471 "CELL SIGNALLING THROUGH mGLU receptors" and Fig. 3).

In the present invention, different kinds of GPCRs can activate Gx, or the specific chimeras recited in the present claims. In other words, one Gx can couple with several kinds of GPCRs. Hermans merely describes that mGluR1 activates Gq, Gi and Gs, or that Gq, Gi and Gs can couple with mGluR1. This difference is illustrated by the figure attached herewith as Exhibit A.

Accordingly, because Nakamura fails to teach or disclose each and every limitation of claims 1 and 5, Nakamura cannot anticipate claims 1 and 5. The rejected dependent claims 2 and 6 by virtue of their dependency from the independent claim 1 or 5 are similarly considered by Applicant to patentably define themselves over the Nakamura reference. As such, claims 1-2 and 5-6 stand in condition for allowance for these very same reasons. Reconsideration and withdrawal of this rejection are respectfully requested.

Response to Rejection Under 35 USC § 103

Claims 3-4 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Nakamura et al., 1996, J. Biochem., 120:996-1001 and MPEP § 2411. Applicant respectfully traverses this rejection for at least the following reasons.

Nakamura is discussed above. Nakamura does not teach or suggest the features set forth in claims 3 and 4. For example, Nakamura does not teach or suggest co-expression of GPCRs with unknown functions and chimeric G-proteins. The present invention surprisingly makes it possible to activate PI turnover by coexpressing an GPCRs and Gx. The GPCRs are not limited to be GPCRs that activate Gq subtype G-protein. They can also be even GPCRs that activate Gi subtype G-protein or several subtypes of G-proteins. In other words, according to the present invention, it is possible to search for a ligand for a GPCR that is not known what subtype of G-protein it can activate by a single assay technique based on PI turnover activation. Such a teaching or suggestion is simply not provided by Nakamura.

As to MPEP § 2411, Applicant respectfully submits that this section deals with "Examination Procedure" and biological deposits and this section is not believed pertinent to the §103 rejection.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

Conclusion

For the reasons presented above, all the claims pending in the application are believed by Applicant to define patentable subject matter and should be passed to issue at the earliest possible time. A Notice of Allowance is requested.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

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October 25, 2005
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